REMARKS

The rejection of claims 1, 3, 4, 6-8, 12 and 13 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,039,981 ("Woo"), is respectfully traversed. The rejection of claims 1, 6 and 7 under 35 USC 102(b) as being anticipated by International Application Publication No. WO 97/44014 ("Baert"), is also respectfully traversed. In addition, the rejection of claims 1-9, 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Baert in view of U.S. Patent Application Publication No. US 2004/0248901 ("Lee"), is respectfully traversed.

In view of the amendment to claim 1 and for the reasons provided below, early allowance of pending claims 1, 3, 5, 7-9, 12 and 13 is respectfully requested.

Firstly, the Examiner's kind attention is directed to the fact that claim 1 has been amended to incorporate the limitations of claims 2, 4 and 6, which claims have now been cancelled.

1). Rejection under 35 U.S.C. 102

The oral composition as now defined in amended claim 1, comprises itraconazole, an acidifying agent selected from the group consisting of phosphoric acid, hydrochloric acid and an aqueous solution thereof, an amphiphilic additive, a surfactant and an oil to form microemulsion in the body fluid when orally administered, and exhibits an itraconazole bioavailability ratio before and after food

ingestion of 0.8 or higher. This is an entirely different composition from that taught by Baert as well as Woo, in that neither teaches the "acidifying agent" component of the composition to form microemulsion in the body fluid when orally administered.

Specifically, the subject composition comprises two separate components, traconazole and an acidifying agent, for dissolving itraconazole, wherein the acidifying agent is selected from the group consisting of phosphoric acid, hydrochloric acid and an aqueous solution thereof. The composition is substantially used as a mixed solvent for dissolving itraconazole together with an amphiphilic additive and a volatile solvent in the preparation of the composition (see lines 12-16 and 30-35, page 3 of the subject specification).

Baert teaches only the fact that itraconazole may be present in the form of an acid addition salt generated using an appropriate acid ("an acid addition salt of itraconazole") (see line 34, page 1 to line 4, page 2 of Baert). In addition, Woo, newly cited in this Office Action, relates to an antifungal composition for oral administration comprising "a fused mixture of itraconazole and phosphoric acid," a pharmaceutically acceptable carrier and a surfactant, the fused mixture of itraconazole and phosphoric acid being obtained by heating a mixture of itraconazole and phosphoric acid to a temperature ranging from 100 to 170℃ (see lines 17 to 25, column 2; lines 14 to 21, column 3; and claims 1 and 5 of Woo).

In other words, the use of said two components, itraconazole and the acidifying agent for dissolving itraconazole in the subject invention, is completely new and different from the uses of "the acid addition salt of itraconazole" mentioned in Baert and from "the fused mixture of itraconazole and phosphoric acid" disclosed in Woo.

Further, the itraconazole composition of the subject invention forms microemulsion in the body fluid when orally administered. In fact, it forms a a liquid phase microemulsion preconcentrate which is viscous, glassy and compact as compared to a conventional microemulsion composition (see lines 30-35, page 5 of the subject specification), and thus forms a highly stable microemulsion in the body fluid which constitutes microemulsion particles in a size range of from several to several ten nm in size when orally administered (see line 36, page 5 to line 2, page 6 of the subject specification), while Baert's and Woo's compositions are both "solid dispersions" (in a solid state as opposed to a liquid or gaseous state).

For all of the above reasons, the rejection of claims 1, 3, 4, 6-8, 12 and 13 under 35 USC 102(b) in view of Woo and the rejection of claims 1, 6 and 7 under 35 USC 102(b) in view of Baert should be withdrawn.

2). <u>Rejection under 35 U.S.C. 103</u>

The Examiner alleged that Lee teaches that an oil such as tocopherol can be used in an itraconazole-containing composition, the subject composition is

obvious over the prior art references by applying the disclosure of Lee to the composition disclosed in Baert.

However, as set forth above, it should be noted that the subject composition further comprises an acidifying agent such as phosphoric acid and hydrochloric acid which is absent in the Baert composition. Thus, even though the Baert composition comprises tocopherol as an oil component, it does not suggest adding an acidifying agent to form a microemulsion in the body fluid.

Furthermore, by providing a high and stable level of itraconazole dissolution rate even under a neutral or alkaline condition of pH 6.8 or higher, the itraconazole bioavailability thereof is little influenced by ingested food (i.e., the itraconazole bioavailability ratio before and after food ingestion is 0.8 or higher), as fully supported by Test Example 1 (dissolution test) and Test Example 2 (in vivo absorption test) of the specification as originally filed. As can be seen from the results, i.e., Tables 1 and 2, of Test Example 1, and as demonstrated in the Inventor's Declaration previously filed, the subject preparation of Example 1 exhibits a higher amount of dissolved itraconazole than those of Comparative Example and the commercially available preparations (in particular, Sporanox® tablet (Janssen Korea), the formulation of the Baert composition) at pH 1.2 or 6.8, and itraconazole bioavailability thereof is much higher and far less influenced by ingested food as compared to that of Sporanox® tablet. This is an unexpected result not taught in the prior art.

In particular, phosphoric acid or hydrochloric acid used as the acidifying agent in the subject composition is a strong acid which greatly contributes to a high itraconazole dissolution rate under an alkaline condition of pH 6.8 or higher. In case of using a relatively weak organic acid instead of a strong acid, in the preparation of the subject composition, the organic acid is not capable of dissolving in a volatile solvent used, which makes its preparation impossible. In addition, it is predicted that even though an itraconazole preparation comprising an organic acid is obtained, the itraconazole dissolution rate thereof will be very low under an alkaline condition due to its limited pH lowering capability.

As described above, it is believed that the subject technical features as well as the aforementioned beneficial effects arising therefrom are not taught, suggested or disclosed by the cited references, even if they are combined.

Therefore, the present invention defined in pending claims 1, 3, 5, 7-9, 12 and 13 is clearly patentable over the cited references, and it is respectfully requested that the rejections of claims 1, 3, 5, 7-9, 12 and 13 under 35 U.S.C. 102 and 103 be withdrawn.

CONCLUSION

Reconsideration and allowance of claims 1, 3, 5, 7-9, 12 and 13 is respectfully solicited.

Respectfully submitted
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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this AMENDMENT is being deposited with the Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via EFS-Web on October 5, 2007.

Signed: _____
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